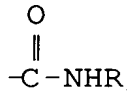
WHAT IS CLAIMED IS:

1. A GnRH antagonist peptide having the formula:

X-D-2Nal-(A)D-Phe-D-3Pal-Ser-Xaa_5-Xaa_6-Leu-Xaa_8-Pro-Xaa_{10}

and the pharmaceutically acceptable salts thereof wherein:

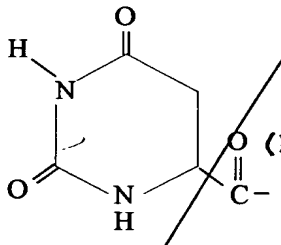
X is an acyl group having not more than carbon atoms or Q,

with Q being  ,

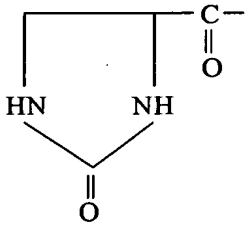
and with R being H or lower alkyl;

A is 4Cl, 4F, 4Br, $4NO_2$, $4CH_3$, $4OCH_3$, $3,4Cl_2$ or $C^{\alpha}Me4Cl$;

Xaa_5 is $4Aph(Q_1)$ or $4Amf(Q_1)$ with Q_1 being Q or

 (D- or L-Hor)

or

 (D- or L-Imz)

Xaa_6 is D-$4Aph(Q_2)$, D-$4Amf(Q_2)$, D-Lys(Nic), D-Cit, D-Hci or D-3Pal, with Q_2 being For, Ac, 3-amino-1,2,4-triazole, or Q_1;

Xaa_8 is Lys(ipr), Arg, Har, $Arg(Et_2)$ or $Har(Et_2)$; and

Xaa_{10} is D-Ala-NH_2, $NHCH_2CH_3$, Gly-NH_2, Ala-NH_2, AzaGly-NH_2, Agl-NH_2, D-Agl-NH_2, Agl(Me)-NH_2 or D-Agl(Me)-NH_2.

2. A GnRH antagonist according to claim 1 wherein Q_1 is Hor.

3. A GnRH antagonist according to claim 2 wherein Q_2 is Q and R is H or methyl.

4. A GnRH antagonist according to claim 2 wherein Xaa_6 is D-4Aph(D-Hor).

5. A GnRH antagonist according to claim 2 wherein X is Ac.

6. A GnRH antagonist according to claim 2 wherein Xaa_8 is Lys(ipr).

7. A GnRH antagonist according to claim 2 wherein Xaa_{10} is D-Ala-NH_2.

8. A GnRH antagonist according to claim 2 wherein X is -$CONHCH_3$.

9. A GnRH antagonist according to claim 1 wherein Xaa_5 is 4Aph(Hor) and Xaa_6 is D-4Aph(Ac), D-4Aph(atz), or D-3Pal.

10. A GnRH antagonist according to claim 1 wherein Xaa_5 is 4Aph(Hor) and Q_2 is Q and R is H or methyl.

11. A GnRH antagonist according to claim 1 wherein Xaa_5 is 4Aph(Hor) and Xaa_6 is D-Cit or D-Hci.

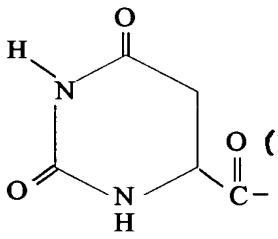
12. A GnRH antagonist according to claim 1 wherein Xaa_5 is 4Aph(carbamoyl) and Xaa_6 is D-4Aph(carbamoyl).

13. A GnRH antagonist peptide according to claim 1 having the formula:
X-D-2Nal-(A)D-Phe-D-3Pal-Ser-Xaa_5-Xaa_6-Leu-Lys(ipr)-Pro-Xaa_{10} wherein:

X is For, Ac, Acr, Pr, Bt, Vl, Vac, Bz or Q,

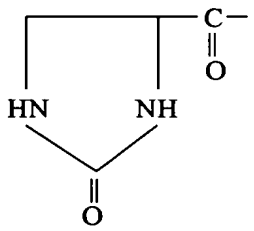
A is 4Cl or 4F;

Xaa_5 is 4Aph(Q_1) or 4Amf(Q_1) with Q_1 being a D-isomer, an L-isomer, or a D/L-isomer mixture of either



(D- or L-Hor)

or



(D- or L-Imz)

Xaa_6 is D-4Aph(Q_2), D-4Amf(Q_2), D-Cit, D-Lys(Nic) or D-3Pal, with Q_2 being For, Ac, Q or Q_1; and

Xaa_{10} is D-Ala-NH_2, $NHCH_2CH_3$ or Gly-NH_2.

14. A GnRH antagonist according to claim 13 wherein Q_1 is Hor and Xaa_6 is D-4Amf(Q), with R being H or methyl.

14

12 15. A GnRH antagonist peptide according to claim 13 wherein X is Ac or Q; R is H or methyl; Xaa_6 is D-4Aph(Q_2), D-4Amf(Q_2) or D-3Pal, with Q_2 being Ac, Q or Q_1; and Xaa_{10} is D-Ala-NH_2.

16. A GnRH antagonist according to claim 1 having the formula: Ac-D-2Nal-D-4ClPhe-D-3Pal-Ser-4Aph(Hor)-Xaa_6-Leu-Lys(ipr)-Pro-D-Ala-NH_2, wherein Xaa_6 is D-4Aph(Ac), D-3Pal, D-4Aph(carbamoyl), D-4Amf(carbamoyl), D-4Amf(methylcarbamoyl) or D-4Aph(D-Hor).

17. A pharmaceutical composition for inhibiting the secretion of gonadotropins in mammals comprising, as an active ingredient, an effective amount of a nontoxic diluent GnRH antagonist according to claim 1 in association with a nontoxic.

18. A method for inhibiting the secretion of gonadotropins in mammals comprising administering an amount of a pharmaceutical composition according to claim 17 which is effective to substantially decrease LH and FSH levels.

19. A GnRH antagonist peptide having the formula:
X-D-2Nal-(A)D-Phe-D-3Pal-Ser-Xaa_5-Xaa_6-Leu-Xaa_8-Pro-Xaa_{10}
and the pharmaceutically acceptable salts thereof wherein:

X is an acyl group having not more than carbon atoms or Q,

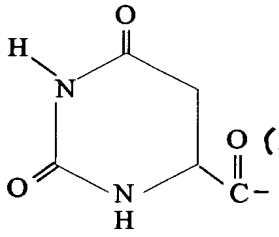
with Q being $-\overset{\overset{O}{\|}}{C}-NHR$,

and with R being H or lower alkyl;

52

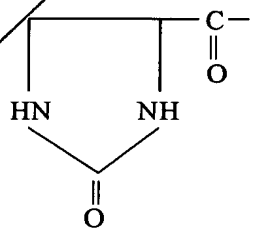
A is 4Cl, 4F, 4Br, $4NO_2$, $4CH_3$, $4OCH_3$, $3,4Cl_2$ or $C^{\alpha}Me4Cl$;

Xaa_5 is $4Aph(Q_1)$ or $4Amf(Q_1)$ with Q_1 being Q, For, Ac, 3-amino-1,2,4-triazole,



(D- or L-Hor)

or



(D- or L-Imz)

Xaa_6 is $D\text{-}4Aph(Q_2)$ or $D\text{-}4Amf(Q_2)$, with Q_2 being Q or D- or L-Hor or D- or L-Imz;

Xaa_8 is Lys(ipr), Arg, Har, diethyl Arg or diethyl Har; and

Xaa_{10} is $D\text{-}Ala\text{-}NH_2$, $NHCH_2CH_3$, $Gly\text{-}NH_2$, $Ala\text{-}NH_2$, $AzaGly\text{-}NH_2$, $Agl\text{-}NH_2$, $D\text{-}Agl\text{-}NH_2$, $Agl(Me)\text{-}NH_2$ or $D\text{-}Agl(Me)\text{-}NH_2$.

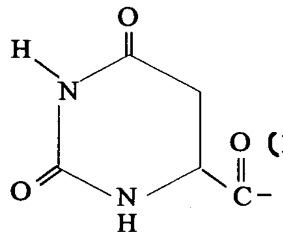
20. An intermediate for making a GnRH antagonist peptide having the formula: X^1-D-2Nal-(A)D-Phe-D-3Pal-Ser(X^2)-Xaa_5-Xaa_6-Leu-Lys(ipr)(X^4)-Pro-X^5 wherein:

X^1 is an α-amino-protecting group;

A is 4Cl or 4F;

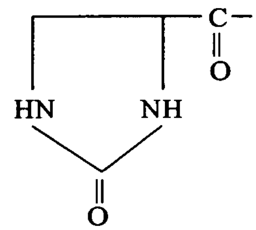
X^2 is an hydroxyl-protecting group;

Xaa_5 is $4Aph(Q_1)$ or $4Amf(Q_1)$ with Q_1 being a D-isomer, an L-isomer or a D/L-isomer mixture of either



(D- or L-Hor)

or



(D- or L-Imz)

Xaa_6 is D-4Aph(Q_2), D-4Amf(Q_2) or D-3Pal, with Q_2 being Ac, Q_1, carbamoyl or methylcarbamoyl;

X^4 is an acid-labile amino-protecting group; and

X^5 is D-Ala-, Gly-, Ala-, Agl-, D-Agl-, Agl(Me)-, or D-Agl(Me)-resin support; or N(Et)-resin support; an amide of D-Ala, Gly or Ala; ethylamide; or AzaGly-NH_2.